

**CLAIMS**

1. A method of diagnosing *Mycobacterium tuberculosis* infection in a human, or  
5 of determining whether a human has been exposed to *Mycobacterium tuberculosis*, comprising:
  - (i) contacting T-cells from said human with one or more of
    - (a) a peptide having the sequence shown in SEQ ID NO: 1;
    - (b) a peptide having or comprising the sequence of at least 8 consecutive amino acids of the sequence shown in SEQ ID NO: 1; or
    - (c) a peptide having or comprising a sequence which is capable of binding to a T-cell receptor which recognises a peptide as defined in (a) or (b); and
  - (ii) determining whether any of the said T-cells recognise said peptide,  
wherein steps (i) and (ii) are optionally carried out *in vitro*.
- 15 2. A method of increasing the sensitivity of a diagnostic test for diagnosing *Mycobacterium tuberculosis* infection in a human, wherein said diagnostic test comprises contacting T cells from said human with a *Mycobacterium tuberculosis* antigen which is not Rv3879c, said method additionally comprising
  - (i) contacting T-cells from said human with one or more of
    - (a) a peptide having the sequence shown in SEQ ID NO: 1;
    - (b) a peptide having or comprising the sequence of at least 8 consecutive amino acids of the sequence shown in SEQ ID NO: 1; or
    - (c) a peptide having or comprising a sequence which is capable of binding to a T-cell receptor which recognises a peptide as defined in (a) or (b); and
  - (ii) determining whether any of the said T-cells recognise said peptide,  
wherein steps (i) and (ii) are optionally carried out *in vitro*.
3. A method according to claim 1 or 2, wherein step (i) further comprises contacting said T-cells with one or more further *Mycobacterium tuberculosis* T-cell antigen(s) or  
30 with an analogue(s) of said antigen(s) which is capable of binding to a T-cell receptor which recognises said antigen(s).
4. A method according to claim 3, wherein said one or more further T-cell

antigens include antigens encoded by the RD-1 or RD-2 region, which antigens are preferably ESAT-6 and/or CFP10; or fragments thereof which are at least 8 amino acids long.

5. A method according to any one of claims 2 to 4, wherein said one or more  
5 further T-cell antigens include Rv3873, Rv3878 or Rv1989c; or fragments thereof which are at  
least 8 amino acids long.

6. A method according to any one of the preceding claims, wherein step (i)  
comprises contacting said sample of T-cells with two or more different peptides, each having the  
10 sequence of at least 8 consecutive amino acids of the sequence shown in SEQ ID NO: 1.

7. A method according to any one of the preceding claims wherein peptides from,  
or analogues of, at least five different antigens are contacted with the T cells.

15 8. A method according to any one of the preceding claims wherein one or more of  
the peptides  
(i) represented by SEQ ID NO's 2 to 18, or  
(ii) which bind to a T-cell which recognise (i), are contacted with the T cells.

20 9. A method according to any one of the preceding claims, wherein recognition of  
said peptide by said T-cells is determined by detecting the secretion of a cytokine from the T-  
cells.

10. A method according to claim 9, wherein the cytokine is IFN- $\gamma$ .

25 11. A method according to claim 9 or 10, wherein said cytokine is detected by  
allowing said cytokine to bind to an immobilised antibody specific to said cytokine and detecting  
the presence of the antibody/cytokine complex.

30 12. A method according to any one of the preceding claims, wherein said T-cells  
are freshly isolated *ex vivo* cells.

13. A method according to any one of claims 1 to 11, wherein said T-cells have been cultured *in vitro*.

14. Use of

- 5 (i) a peptide as defined in claim 1 or 8, and optionally also an antigen as defined in any one of claims 3 to 5, or  
(ii) a polynucleotide which is capable of expressing (i),  
in the manufacture of a diagnostic means for diagnosing *Mycobacterium tuberculosis* infection or exposure in a human.

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15. A diagnostic composition comprising a peptide as defined in claim 1 or 8 and optionally one or more further *Mycobacterium tuberculosis* T-cell antigens.

16. A composition according to claim 15 wherein said one or more further T-cell  
15 antigens are selected from

- (i) ESAT-6, CFP10, Rv3873, Rv3878, Rv1989c or fragment of any thereof which is at least 8 amino acids long; or  
(ii) an analogue of (i) which binds to a T-cell which recognises (i).

20 17. A kit for diagnosing *Mycobacterium tuberculosis* infection or exposure in a human, comprising one or more peptides as defined in claim 1 or 8 or a composition according to claim 15 or 16, and optionally a means for detecting recognition of a peptide by T-cells.

18. A kit according to claim 17, wherein said means for detecting recognition of a  
25 peptide by T-cells comprises an antibody to a cytokine.

19. A kit according to claim 18, wherein said antibody is immobilised on a solid support and wherein said kit optionally comprises a means to detect an antibody/cytokine complex.

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20. A kit according to claim 18 or 19, wherein said cytokine is IFN- $\gamma$ .

21. A method of ascertaining the stage of a *Mycobacterium tuberculosis* infection in a human comprising determining whether there is a differential T cell response to different antigens in the human.

5 22. A method according to claim 21 wherein T cell responses to one or more of Rv3879c, ESAT-6, CFP10, Rv3873, Rv3878, Rv1989c are measured.

10 23. A method according to claim 21 or 22 which is carried out to  
(i) to determine whether the infection is recent or longstanding, or  
(ii) to determine whether the human is latently infected or has disease, or  
(iii) to monitor the effect of treatment.